

SYMBOL	AMINO ACID
Y	L-tyrosine
G	glycine
F	L-phenylalanine
M	L-methionine
A	L-alanine
S	L-serine
I	L-isoleucine
L	L-leucine
T	L-threonine
V	L-valine
P	L-proline
K	L-lysine
H	L-histidine
Q	L-glutamine
E	L-glutamic acid
W	L-tryptophan
R	L-arginine
D	L-aspartic acid
N	L-asparagine
C	L-cysteine

FIG. 1



SEQ ID. NO. 1 =  
N-terminal DICNTMHYTNWTHIYICEE C-terminal

SEQ ID. NO. 2 =  
N-terminal HKSAIVTLTYDSEWQR C-terminal

SEQ. ID. NOS. 1 and 2, denoted by underlining, are attributed to the E2 coding region of HPV-16 as follows::

	5	10	15	20	25	30
1	M	E	T	L	C	Q
	R	L	N	V	C	Q
	D	K	I	L	T	H
	Y	E	N	D	S	T
	D	L	R	D	H	I
31	D	Y	W	K	H	M
	R	L	E	C	A	I
	Y	Y	K	A	R	E
	M	G	F	K	H	I
	N	H	Q	V	V	P
61	T	L	A	V	S	K
	N	K	A	L	Q	A
	I	E	L	Q	L	T
	L	E	T	I	Y	N
	S	Q	Y	S	N	E
91	K	W	T	L	Q	D
	V	S	L	E	V	Y
	L	T	A	P	T	G
	C	I	K	K	H	G
	Y	T	V	E	V	Q
121	F	D	G	D	I	C
	N	T	M	H	Y	T
	N	W	T	H	I	Y
	I	C	E	E	A	S
	V	T	V	V	E	G
151	Q	V	D	Y	Y	G
	L	Y	V	H	E	G
	I	R	T	Y	F	V
	Q	F	K	D	D	A
	E	K	Y	S	K	
181	N	K	V	W	E	V
	H	A	G	G	Q	V
	I	L	C	P	T	S
	V	F	S	S	N	E
	V	S	S	P	E	I
211	I	R	Q	H	L	A
	N	H	P	A	A	T
	H	T	K	A	V	A
	L	G	T	E	E	T
	Q	T	T	I	Q	R
241	P	R	S	E	P	D
	T	G	N	P	C	H
	T	T	K	L	L	H
	R	D	S	V	D	S
	A	P	I	L	T	A
271	F	N	S	S	H	K
	G	R	I	N	C	N
	S	N	T	T	P	I
	V	H	L	K	G	D
	A	N	T	L	K	C
301	L	R	Y	R	F	K
	K	H	C	T	L	Y
	T	A	V	S	S	T
	W	H	W	T	G	H
	N	V	K	H	K	S
331	A	I	V	T	L	T
	Y	D	S	E	W	Q
	R	D	Q	F	L	S
	Q	V	K	I	P	K
	T	I	T	V	S	T
361	G	F	M	S	I	

FIG. 2

SEQ ID. NO. 3 =

N-terminal PTLHEYMLDLQPETTDLYCYEQLNDSSEE C-terminal

SEQ ID. NO. 4 =

N-terminal CDSTLRRLCVQSTHVDIRTLE C-terminal

Sequence ID. NOs. 3 and 5, denoted by underlining, are attributed to the E7 coding region of HPV-16 as follows:

	5	10	15	20	25	30																								
1	M	H	G	D	T	<u>P</u>	<u>T</u>	<u>L</u>	<u>H</u>	<u>E</u>	<u>Y</u>	<u>M</u>	<u>L</u>	<u>D</u>	<u>L</u>	<u>Q</u>	<u>P</u>	<u>E</u>	<u>T</u>	<u>T</u>	<u>D</u>	<u>L</u>	<u>Y</u>	<u>C</u>	<u>Y</u>	<u>E</u>	<u>Q</u>	<u>L</u>	<u>N</u>	<u>D</u>
31	<u>S</u>	<u>S</u>	<u>E</u>	<u>E</u>	<u>E</u>	<u>D</u>	<u>E</u>	<u>I</u>	<u>D</u>	<u>G</u>	<u>P</u>	<u>A</u>	<u>G</u>	<u>Q</u>	<u>A</u>	<u>E</u>	<u>P</u>	<u>D</u>	<u>R</u>	<u>A</u>	<u>H</u>	<u>Y</u>	<u>N</u>	<u>I</u>	<u>V</u>	<u>T</u>	<u>F</u>	<u>C</u>	<u>C</u>	<u>K</u>
61	<u>C</u>	<u>D</u>	<u>S</u>	<u>T</u>	<u>L</u>	<u>R</u>	<u>L</u>	<u>C</u>	<u>V</u>	<u>Q</u>	<u>S</u>	<u>T</u>	<u>H</u>	<u>V</u>	<u>D</u>	<u>I</u>	<u>R</u>	<u>T</u>	<u>L</u>	<u>E</u>	<u>D</u>	<u>L</u>	<u>L</u>	<u>M</u>	<u>G</u>	<u>T</u>	<u>L</u>	<u>G</u>	<u>I</u>	<u>V</u>
91	C	P	I	C	S	Q	K	P																						

FIG. 3

SEQ ID. NO. 5 =

N-terminus EKTGILTVTYHSETQRTKFC-terminus

SEQ ID. NO. 5, denoted by underlining, is attributed to the E2 coding region of HPV-18 as follows:

	5	10	15	20	25	30																								
1	M	Q	T	P	K	E	T	L	S	E	R	L	S	C	V	Q	D	K	I	I	D	H	Y	E	N	D	S	K	D	I
31	D	S	Q	I	Q	Y	W	Q	L	I	R	W	E	N	A	I	F	F	A	A	R	E	H	G	I	Q	T	L	N	H
61	Q	V	V	P	A	Y	N	I	S	K	S	K	A	H	K	A	I	E	L	Q	M	A	L	Q	G	L	A	Q	S	R
91	Y	K	T	E	D	W	T	L	Q	D	T	C	E	E	L	W	N	T	E	P	T	H	C	F	K	K	G	G	Q	T
121	V	Q	V	Y	F	D	G	N	K	D	N	C	M	T	Y	V	A	W	D	S	V	Y	Y	M	T	D	A	G	T	W
151	D	K	T	A	T	C	V	S	H	R	G	L	Y	Y	V	K	E	G	Y	N	T	F	Y	I	E	F	K	S	E	C
181	E	K	Y	G	N	T	G	T	W	E	V	H	F	G	N	N	V	I	D	C	N	D	S	M	C	S	T	S	D	D
211	T	V	S	A	T	Q	L	V	K	Q	L	Q	H	T	P	S	P	Y	S	S	T	V	S	V	G	T	A	K	T	Y
241	G	Q	T	S	A	A	T	R	P	G	H	C	G	L	A	E	K	Q	H	C	G	P	V	N	P	L	L	G	A	A
271	T	P	T	G	N	N	K	R	R	K	L	C	S	G	N	T	T	P	I	I	H	L	K	G	D	R	N	S	L	K
301	C	L	R	Y	R	L	R	K	H	S	D	H	Y	R	D	I	S	S	T	W	H	W	T	G	A	G	N	<u>E</u>	<u>K</u>	<u>T</u>
331	<u>G</u>	<u>I</u>	<u>L</u>	<u>T</u>	<u>V</u>	<u>T</u>	<u>Y</u>	<u>H</u>	<u>S</u>	<u>E</u>	<u>T</u>	<u>Q</u>	<u>R</u>	<u>T</u>	<u>K</u>	<u>F</u>	<u>L</u>	<u>N</u>	<u>T</u>	<u>V</u>	<u>A</u>	<u>I</u>	<u>P</u>	<u>D</u>	<u>S</u>	<u>V</u>	<u>Q</u>	<u>I</u>	<u>L</u>	<u>V</u>
361	G	Y	M	T	M																									

FIG. 4

**TABLE 1. Serum Immunoassays Employing Peptides of Invention.** These assays are compared against Pap cytology and HPV DNA Hybrid Capture analyses of cervical cells from the same patients. Serum and cervical cells were taken from participants by a gynecological physician. Pap smears and the Digene HPV DNA Assays<sup>1</sup> were processed at a certified clinical laboratory. Prior to completion of this trial, persons doing the Impact Diagnostics HPV Immunoassay were not informed of the results of other assays or of participant histories. Unless otherwise specified, participants were more than 35 years old. KEY: pos = positive; neg = negative; n/a = not applicable or not done; insufficient = insufficient number of cells for analysis

Sample	Pap Smear	Digene HPV DNA Assay	Impact HPV Immunoassay <sup>2</sup>			Comments
			HPV-16a	HPV-16b	HPV-18	
1	neg	n/a	pos	pos	neg	CERVICAL CANCER diagnosed in 1987; surgical removal of lesion
2	n/a	n/a	pos	pos	pos	CERVICAL CANCER diagnosed in 1991; total hysterectomy
3	neg	neg	pos	neg	pos	Previous Pap Smear -- CIN III <sup>3</sup>
4	neg	neg	pos	neg	pos	Previous Pap Smear -- CIN III <sup>3</sup>
5	neg	Insufficient	neg	neg	pos	Previous Pap Smear -- CIN I <sup>3</sup>
6	neg	neg	neg	pos	pos	Previous Pap Smear -- CIN I <sup>3</sup>
7	neg	neg	pos	pos	pos	Previous Pap Smear -- CIN I <sup>3</sup>
8	neg	neg	pos	neg	pos	Previous Pap Smear -- CIN I-II <sup>3</sup>
9	neg	neg	neg	neg	pos	No history of abnormal Pap Smears; multiple sex partners confirmed
10	neg	neg	pos	pos	neg	No history of abnormal Pap Smears
11	neg	neg	pos	pos	pos	No history of abnormal Pap Smears; multiple sex partners confirmed
12	neg	neg	pos	pos	pos	No history of abnormal Pap Smears;
13	neg	neg	pos	neg	neg	No history of abnormal Pap Smears;
14	neg	neg	neg	neg	pos	No history of abnormal Pap Smears
15	ASCUS <sup>3</sup>	pos	neg	pos	neg	No history of abnormal Pap Smears
16	neg	neg	pos	pos	neg	No history of abnormal Pap Smears
17	n/a	n/a	pos	neg	neg	Promiscuous woman
18	n/a	n/a	pos	neg	neg	Promiscuous woman
19	neg	neg	neg	neg	neg	Virgin -- 14 years old
20	neg	neg	neg	neg	neg	Virgin -- 15 years old
21	neg	n/a	neg	neg	neg	No history of abnormal Pap Smears; multiple sex partners confirmed
22	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
23	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
24	neg	neg	neg	neg	neg	No history of abnormal Pap Smears

**FIG. 5**

TABLE 1. Serum Immunoassays Employing Peptides of Invention. Continued

Sample	Pap Smear	Digene HPV DNA Assay	Impact HPV Immunoassay <sup>2</sup>			Comments
			HPV-16a	HPV-16b	HPV-18	
25	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
26	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
27	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
28	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
29	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
30	neg	neg	neg	neg	neg	No history of abnormal Pap Smears
31	neg	neg	neg	neg	neg	No history of abnormal Pap Smears

<sup>1</sup> The Digene HPV DNA Assay requires a substantial number of cells for successful detection of HPV DNA. Also, it only finds HPV DNA when the virus is abundantly proliferating (and not when infections are dormant).

<sup>2</sup> HPV-16a = Epitope for the E2 Region of HPV-16; HPV-16b = Epitope for the E7 Region of HPV-16; HPV-18 = Epitope for the E2 Region of HPV-18. For the HPV Immunoassay, a positive result is visually expressed by a prominent BLUE color and a negative one by remaining COLORLESS.

<sup>3</sup> ASCUS refers to unusual or atypical cells in a Pap Smear. These are usually of undetermined significance and most often turn out to be inconsequential. In *mild dysplasia* (CIN I), only a few cells are abnormal, while in *moderate dysplasia* (CIN II) the abnormal cells involve about one-half of the thickness of the surface lining of the cervix. In *severe dysplasia* or *carcinoma-in-situ* (CIN III), the entire thickness of cells is disordered, but the abnormal cells have not yet spread below the surface. Carcinoma-in-situ means "cancer in place". If this condition is not treated, it often will grow into *invasive cancer*. In dysplasia and carcinoma-in-situ all of the abnormalities are confined to the surface lining (or "skin") of the cervix. For invasive cancer, the cells are not only disordered throughout the entire thickness of the lining, but they invade the tissue underlying the surface.

FIG. 6